

75288

STIC-Biotech/ChemLib

From: Portner, Ginny  
Sent: Tuesday, September 10, 2002 1:09 PM  
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Please search SEQ ID NOs 1,3 and 5.

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TYPE OF SEARCH:  
NA Sequences: 3  
AA Sequences: \_\_\_\_\_  
Structures: \_\_\_\_\_  
Bibliographic: \_\_\_\_\_  
Litigation: \_\_\_\_\_  
Full text: \_\_\_\_\_  
Patent Family: \_\_\_\_\_  
Other: \_\_\_\_\_

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Pending Nucleic Acid and/or Pending Amino Acid database searches now generate two sets of results. These databases were split into two parts to reduce the time needed to update the databases daily. The split freed up more machine time for processing searches.

Searches run against the Nucleic Acid Pending database produce two sets of results, with the extensions, **.rnpm** and **.rnpn**

Searches run against the Amino Acid Pending database produce two sets of results, with the extensions, **.rapm** and **.rapn**

*The Pending database search results should not be left in the case because they contain data that is confidential.*

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## General information about the entry

Entry name **BXA1\_CLOBO**  
 Primary accession number **P10845**  
 Secondary accession numbers **P18639 P01561**  
 Entered in SWISS-PROT in **Release 11, July 1989**  
 Sequence was last modified in **Release 26, July 1993**  
 Annotations were last modified in **Release 41, June 2002**

## Name and origin of the protein

Protein name **Botulinum neurotoxin type A [Precursor]**  
 Synonyms **EC 3.4.24.69**  
**BoNT/A**  
**Bontoxilysin A**  
**BOTOX**  
 Contains **Botulinum neurotoxin A, light-chain**  
**Botulinum neurotoxin A, heavy-chain**  
 Gene name **BOTA or BNA or ATX**  
 From **Clostridium botulinum [TaxID: 1491]**  
 Taxonomy **Bacteria; Firmicutes; Clostridia; Clostridiales; Clostridiaceae; Clostridium.**

## References

### [1] SEQUENCE FROM NUCLEIC ACID.

**STRAIN=NCTC 2916;**  
 MEDLINE=90235864; PubMed=2185020; [[NCBI](#), [ExPASy](#), [EBI](#), [Israel](#), [Japan](#)]  
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"Organization and phylogenetic interrelationships of genes encoding components of the botulinum toxin complex in proteolytic *Clostridium botulinum* types A, B, and F: evidence of chimeric sequences in the gene encoding the nontoxic nonhemagglutinin component.";

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"Crystal structure of botulinum neurotoxin type A and implications for toxicity.";

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**Comments**

- **FUNCTION:** Inhibits acetylcholine release. The botulinum toxin binds with high affinity to peripheral neuronal presynaptic membrane, is then internalized by receptor-mediated endocytosis. The C-terminus of the heavy chain (H) is responsible for the adherence of the toxin to the cell surface while the N-terminus mediates transport of the light chain from the endocytic vesicle to the cytosol. After translocation, the light chain (L) hydrolyzes the 197-Gln-|-Arg-198 bond in SNAP-25, thereby blocking neurotransmitter release. Inhibition of acetylcholine release results in flaccid paralysis, with frequent heart or respiratory failure.
- **CATALYTIC ACTIVITY:** Limited hydrolysis of proteins of the neuroexocytosis apparatus, synaptobrevins, SNAP25 or syntaxin. No detected action on small molecule substrates.
- **SUBUNIT:** Disulfide-linked heterodimer of a light chain (L) and a heavy chain (H).
- **SUBCELLULAR LOCATION:** Secreted.
- **PHARMACEUTICAL:** Available under the name BOTOX (Allergan) for the treatment of strabismus and blepharospasm associated with dystonia and cervical dystonia. Also used for the treatment of hemifacial spasm and a number of other neurological disorders characterized by abnormal muscle contraction.
- **MISCELLANEOUS:** There are seven antigenically distinct forms of botulinum neurotoxin: Types A, B, C1, D, E, F, and G.
- **SIMILARITY:** BELONGS TO PEPTIDASE FAMILY M27.
- **DATABASE:** NAME=BOTOX product information Web site; WWW="<http://www.botox.com/index.jsp?hp&productinfo>".
- **DATABASE:** NAME=Protein Spotlight; NOTE=Issue 19 of February 2002; WWW="<http://www.expasy.org/spotlight/articles/sptlt019.html>".

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### Cross-references

EMBL	X52066; CAA36289.1; -. [ <a href="#">EMBL</a> / <a href="#">GenBank</a> / <a href="#">DDBJ</a> ] [ <a href="#">CoDingSequence</a> ] M30196; AAA23262.1; -. [ <a href="#">EMBL</a> / <a href="#">GenBank</a> / <a href="#">DDBJ</a> ] [ <a href="#">CoDingSequence</a> ] X92973; CAA63551.1; -. [ <a href="#">EMBL</a> / <a href="#">GenBank</a> / <a href="#">DDBJ</a> ] [ <a href="#">CoDingSequence</a> ] D67030; BAA11051.1; -. [ <a href="#">EMBL</a> / <a href="#">GenBank</a> / <a href="#">DDBJ</a> ] [ <a href="#">CoDingSequence</a> ] M27892; AAA23269.1; -. [ <a href="#">EMBL</a> / <a href="#">GenBank</a> / <a href="#">DDBJ</a> ] [ <a href="#">CoDingSequence</a> ]
PIR	A35294; BTCLAB. S09492; S09492.
PDB	3BTA; 01-OCT-99.[ <a href="#">ExPASy</a> / <a href="#">RCSB</a> ]
MEROPS	<a href="#">M27.002</a> ; -. <a href="#">IPR000395</a> ; <a href="#">Bontoxilysin</a> . <a href="#">IPR000130</a> ; <a href="#">Zn_MTpeptdse</a> . <a href="#">Graphical view of domain structure</a> .
Pfam	<a href="#">PF01742</a> ; <a href="#">Peptidase_M27</a> ; 1.
PRINTS	<a href="#">PR00760</a> ; <a href="#">BONTOXILYSIN</a> .
ProDom	<a href="#">PD001963</a> ; <a href="#">Bontoxilysin</a> ; 1. <a href="#">[Domain structure / List of seq. sharing at least 1 domain]</a> .
PROSITE	<a href="#">PS00142</a> ; <a href="#">ZINC_PROTEASE</a> ; 1.
BLOCKS	<a href="#">P10845</a> .
ProtoNet	<a href="#">P10845</a> .
ProtoMap	<a href="#">P10845</a> .
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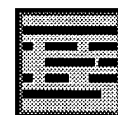
### Keywords

**Neurotoxin; Transmembrane; Hydrolase; Metalloprotease; Zinc; Pharmaceutical; 3D-structure.**

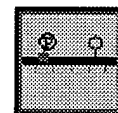
### Features

Key	From	To	Length	Description
INIT_MET	0	0		
CHAIN	<a href="#">1</a>	<a href="#">447</a>	447	BOTULINUM NEUROTOXIN A, LIGHT-CHAIN.
CHAIN	<a href="#">448</a>	<a href="#">1295</a>	848	BOTULINUM NEUROTOXIN A, HEAVY-CHAIN.
METAL	<a href="#">222</a>	<a href="#">222</a>		ZINC (CATALYTIC).
ACT_SITE	<a href="#">223</a>	<a href="#">223</a>		
METAL	<a href="#">226</a>	<a href="#">226</a>		ZINC (CATALYTIC).
METAL	<a href="#">261</a>	<a href="#">261</a>		ZINC (CATALYTIC).
DISULFID	<a href="#">429</a>	<a href="#">453</a>		INTERCHAIN.
DISULFID	<a href="#">1234</a>	<a href="#">1279</a>		
TRANSMEM	<a href="#">626</a>	<a href="#">646</a>	21	POTENTIAL.
TRANSMEM	<a href="#">655</a>	<a href="#">675</a>	21	POTENTIAL.
VARIANT	<a href="#">26</a>	<a href="#">26</a>		V -> A.
MUTAGEN	<a href="#">261</a>	<a href="#">261</a>		

E->A: DRASTIC DECREASE IN



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MUTAGEN	<u>265</u>	<u>265</u>	ENZYMATIC ACTIVITY. F->A: DECREASE IN ENZYMATIC ACTIVITY.
MUTAGEN	<u>365</u>	<u>365</u>	Y->A: DECREASE IN ENZYMATIC ACTIVITY.
CONFLICT	<u>1</u>	<u>1</u>	P -> Q (IN REF. <u>1</u> ).
CONFLICT	<u>479</u>	<u>479</u>	E -> P (IN REF. <u>9</u> ).
CONFLICT	<u>875</u>	<u>875</u>	T -> L (IN REF. <u>8</u> ).
CONFLICT	<u>891</u>	<u>891</u>	S -> K (IN REF. <u>8</u> ).

**Sequence information**Length: **1295 AA** [This is the length of the unprocessed precursor]Molecular weight: **149322 Da** [This is the MW of the unprocessed precursor]CRC64: **858342F754862579** [This is a checksum on the sequence]

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70	80	90	100	110	120
PPEAKQVPVS	YYDSTYLSTD	NEKDNYLKGV	TKLFERIYST	DLGRMLLTSI	VRGIPFWGGS
130	140	150	160	170	180
TIDTELKVID	TNCINVIQPD	GSYRSEELNL	VIIGPSADII	QFECKSFGHE	VLNLTRNGYG
190	200	210	220	230	240
STQYIRFSPD	FTFGFEESLE	VDTNPLLGA	KFATDPAVTL	AHELIHAGHR	LYGIAINPNR
250	260	270	280	290	300
VFKVNTNAYY	EMSGLEVSFE	ELRTFGGHDA	KFIDSLQENE	FRLYYYNKFK	DIASLTNKA
310	320	330	340	350	360
SIVGTTASLQ	YMKNVFKEY	LLSEDTSKGF	SVDKLKFDKL	YKMLTEIYTE	DNFVKFFKVL
370	380	390	400	410	420
NRKTYLNFDK	AVFKINIVPK	VNYTIYDGFN	LRNTNLAANF	NGQNTNINNM	NFTKLKNFTG
430	440	450	460	470	480
LFEFYKLLCV	RGIITSKTKS	LDKGYNKALN	DLCIKVNNWD	LFFSPSEDNF	TNDLNKGEEI
490	500	510	520	530	540
TSDTNIEAAE	ENISLDLIQQ	YYLTFNFDNE	PENISIENLS	SDIIGQLELM	PNIERFPNGK
550	560	570	580	590	600
KYELDKYTMF	HYLRAQEFEH	GKSRIALTNS	VNEALLNPSR	VYTFSSDYV	KKVNKATEAA
610	620	630	640	650	660
MFLGWVEQLV	YDFTDETSEV	STTDKIADIT	IIIPYIGPAL	NIGNMLYKDD	FVGALIFSGA

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      670      680      690      700      710      720
      |      |      |      |      |      |
VILFEIPEI AIPVLGTFAL VSYIANKVLT VQTIDNALSK RNEKWDEVYK YIVTNWLAKV

      730      740      750      760      770      780
      |      |      |      |      |      |
NTQIDLIRKK MKEALENQAE ATKAIINYQY NQYTEEEKNN INFNIDDLSS KLNESINKAM

      790      800      810      820      830      840
      |      |      |      |      |      |
ININKFLNQC SVSYLMNSMI PYGVKRLDF DASLKDALLK YIIDNRGTLI GQVDRCLKDKV

      850      860      870      880      890      900
      |      |      |      |      |      |
NNTLSTDIPF QLSKYVDNQR LLSTFTEYIK NIINTSILNL RYESNHLIDL SRYASKINIG

      910      920      930      940      950      960
      |      |      |      |      |      |
SKVNFDPIDK NQIQLFNLES SKIEVILKNA IVYNSMYENF STSFWIRIPK YFNSISLNNE

      970      980      990     1000     1010     1020
      |      |      |      |      |      |
YTIINCMENN SGWKVSLNYG EIIWTLQDTQ EIKQRVVFYK SQMINISDYI NRWIFVTITN

     1030     1040     1050     1060     1070     1080
      |      |      |      |      |      |
NRLNNSKIYI NGRLLIDQKPI SNLGNIHASN NIMFKLDGCR DTHRYIWIKY FNLFDKELNE

     1090     1100     1110     1120     1130     1140
      |      |      |      |      |      |
KEIKDLYDNQ SNSGILKDFW GDYLYQDKPY YMLNLYDPNK YVDVNNVGIR GYMYLKGPRG

     1150     1160     1170     1180     1190     1200
      |      |      |      |      |      |
SVMTTNIYLN SSLYRGTKFI IKKYASGNKD NIVRNNDRVY INVVVKNKEY RLATNASQAG

     1210     1220     1230     1240     1250     1260
      |      |      |      |      |      |
VEKILSALEI PDVGNLSQVV VMKSKNDQGI TNKCKMNLQD NNGNDIGFIG FHQFNNAKL

     1270     1280     1290
      |      |      |
VASNWNRQI ERSSRTLGC WEFIPVDDGW GERPL

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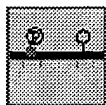


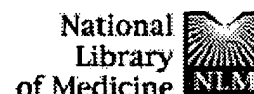
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Tools Sequence analysis tools: [ProtParam](#), [ProtScale](#),  
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- ☐ **1:** East AK, Bhandari M, Stacey JM, Campbell KD, Collins MD. Related Articles, **NEW** Links

Organization and phylogenetic interrelationships of genes encoding components of the botulinum toxin complex in proteolytic *Clostridium botulinum* types A, B, and F: evidence of chimeric sequences in the gene encoding the nontoxic nonhemagglutinin component.

Int J Syst Bacteriol. 1996 Oct;46(4):1105-12.

PMID: 8863443 [PubMed - indexed for MEDLINE]

- ☐ **2:** Santos-Buelga JA, Collins MD, East AK. Related Articles, **NEW** Links

Characterization of the genes encoding the botulinum neurotoxin complex in a strain of *Clostridium botulinum* producing type B and F neurotoxins.

Curr Microbiol. 1998 Nov;37(5):312-8.

PMID: 9767710 [PubMed - indexed for MEDLINE]

- ☐ **3:** Hutson RA, Zhou Y, Collins MD, Johnson EA, Hatheway CL, Sugiyama H. Related Articles, **NEW** Links

Genetic characterization of *Clostridium botulinum* type A containing silent type B neurotoxin gene sequences.

J Biol Chem. 1996 May 3;271(18):10786-92.

PMID: 8631890 [PubMed - indexed for MEDLINE]

- ☐ **4:** Bhandari M, Campbell KD, Collins MD, East AK. Related Articles, **NEW** Links

Molecular characterization of the clusters of genes encoding the botulinum neurotoxin complex in *Clostridium botulinum* (*Clostridium argentinense*) type G and nonproteolytic *Clostridium botulinum* type B.

Curr Microbiol. 1997 Oct;35(4):207-14.

PMID: 9290060 [PubMed - indexed for MEDLINE]

- ☐ **5:** Rodriguez Jovita M, Collins MD, East AK. Related Articles, **NEW** Links

Gene organization and sequence determination of the two botulinum neurotoxin gene clusters in *Clostridium botulinum* type A(B) strain NCTC 2916.

Curr Microbiol. 1998 Apr;36(4):226-31.

PMID: 9504990 [PubMed - indexed for MEDLINE]

- ☐ **6:** East AK, Bhandari M, Hielm S, Collins MD. Related Articles, **NEW** Links

Analysis of the botulinum neurotoxin type F gene clusters in proteolytic and nonproteolytic *Clostridium botulinum* and *Clostridium baratii*.

Curr Microbiol. 1998 Oct;37(4):262-8.

PMID: 9732534 [PubMed - indexed for MEDLINE]

- ☐ **7:** [Kubota T, Yonekura N, Hariya Y, Isogai E, Isogai H, Amano K, Fujii N.](#) [Related Articles](#), [NEW](#) [Links](#)  
Gene arrangement in the upstream region of Clostridium botulinum type E and Clostridium butyricum BL6340 progenitor toxin genes is different from that of other types.  
FEMS Microbiol Lett. 1998 Jan 15;158(2):215-21.  
PMID: 9465394 [PubMed - indexed for MEDLINE]
- ☐ **8:** [Yang GH, Rhee SD, Jung HH, Jhee OH, Yang KH.](#) [Related Articles](#), [NEW](#) [Links](#)  
Cloning and characterization of the upstream region of Clostridium botulinum type B neurotoxin gene.  
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PMID: 7570637 [PubMed - indexed for MEDLINE]

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PMID: 8876967 [PubMed - indexed for MEDLINE]

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PMID: 9434146 [PubMed - indexed for MEDLINE]

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 DT 02-DEC-1996 (Rel. 50, Last updated, Version 5)  
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 RA East A.K., Bhandari M., Stacey J.M., Campbell K.D., Collins M.D.;  
 RT "Organization and phylogenetic interrelationships of genes encoding  
 RT components of the botulinum toxin complex in proteolytic Clostridium  
 RT botulinum types A, B and F: Evidence of chimeric sequences in the gene  
 RT encoding the nontoxic-nonhemagglutinin component";  
 RL Int. J. Syst. Bacteriol. 46:1105-1112(1996).  
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 RL A.K. East, AFRC Inst. of Food Research, Reading Laboratory, Microbiology  
 RL Dept., Earley Gate, Whiteknights Rd., Reading RG6 2bz, UK  
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# SWISS-PROT: BXA1\_CLOBO

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CHAIN 448 1295 BOTULINUM NEUROTOXIN A, HEAVY-CHAIN.

In one-letter code:

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[EMBNET-CH/SIB \(Switzerland\)](#)



Direct BLAST submission at [NCBI \(Bethesda, USA\)](#)



[ScanProsite](#)

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Sequence analysis tools: [ProtParam](#), [ProtScale](#),  
[Compute pI/Mw](#), [PeptideMass](#), [PeptideCutter](#),  
[Dotlet \(Java\)](#)



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 RT comparison with other Clostridial neurotoxins";  
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# SWISS-PROT: P10845

*NiceProt - a user-friendly view of this SWISS-PROT entry*

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DT 01-JUL-1993 (Rel. 26, Last sequence update)  
DT 15-JUN-2002 (Rel. 41, Last annotation update)  
DE Botulinum neurotoxin type A precursor (EC 3.4.24.69) (BoNT/A)  
DE (Bontoxilysin A) (BOTOX) [Contains: Botulinum neurotoxin A, light-  
DE chain; Botulinum neurotoxin A, heavy-chain].  
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RA Thompson D.E., Brehm J.K., Oultram J.D., Swinfield T.-J.,  
RA Shone C.C., Atkinson T., Melling J., Minton N.P.;  
RT "The complete amino acid sequence of the Clostridium botulinum type A  
RT neurotoxin, deduced by nucleotide sequence analysis of the encoding  
RT gene.";  
RL Eur. J. Biochem. 189:73-81(1990).  
RN [2]  
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RC STRAIN=62A;  
RX MEDLINE=90264400; PubMed=2160960; [NCBI, ExPASy, EBI, Israel, Japan]  
RA Binz B., Kuarzono H., Wille M., Frevent J., Wernars K., Niemann H.;  
RT "The complete sequence of botulinum neurotoxin type A and comparison  
RT with other clostridial neurotoxins.";  
RL J. Biol. Chem. 265:9153-9158(1990).  
RN [3]  
RP SEQUENCE OF 1-65 FROM N.A.  
RC STRAIN=62A;  
RX MEDLINE=97016817; PubMed=8863443; [NCBI, ExPASy, EBI, Israel, Japan]  
RA East A.K., Bhandari M., Stacey J.M., Campbell K.D., Collins M.D.;  
RT "Organization and phylogenetic interrelationships of genes encoding  
RT components of the botulinum toxin complex in proteolytic Clostridium  
RT botulinum types A, B, and F: evidence of chimeric sequences in the  
RT gene encoding the nontoxic nonhemagglutinin component.";  
RL Int. J. Syst. Bacteriol. 46:1105-1112(1996).  
RN [4]  
RP SEQUENCE OF 1-34 FROM N.A.  
RC STRAIN=Hall;  
RX MEDLINE=89350959; PubMed=2669749; [NCBI, ExPASy, EBI, Israel, Japan]  
RA Betley M.J., Somers E., Dasgupta B.R.;  
RT "Characterization of botulinum type A neurotoxin gene: delineation of

RT the N-terminal encoding region.";  
RL Biochem. Biophys. Res. Commun. 162:1388-1395(1989).  
RN [5]  
RP SEQUENCE OF 1-18 FROM N.A.  
RC STRAIN=Type A NIH;  
RX MEDLINE=96096783; PubMed=8521962; [NCBI, ExpASY, EBI, Israel, Japan]  
RA Fujita R., Fujinaga Y., Inoue K., Nakajima H., Kumon H., Oguma K.;  
RT "Molecular characterization of two forms of nontoxic-nonhemagglutinin  
RT components of Clostridium botulinum type A progenitor toxins.";  
RL FEBS Lett. 376:41-44(1995).  
RN [6]  
RP SEQUENCE OF 1-16.  
RX MEDLINE=84178501; PubMed=6370252; [NCBI, ExpASY, EBI, Israel, Japan]  
RA Schmidt J.J., Sartymoorthy V., Dasgupta B.R.;  
RT "Partial amino acid sequence of the heavy and light chains of  
RT botulinum neurotoxin type A.";  
RL Biochem. Biophys. Res. Commun. 119:900-904(1984).  
RN [7]  
RP SEQUENCE OF 1-46.  
RA Dasgupta B.R., Foley J., Niece R.;  
RT "Partial sequence of the light chain of botulinum neurotoxin type A.";  
RL Biochemistry 26:4162-4162(1987).  
RN [8]  
RP SEQUENCE OF 1-5 AND 444-456.  
RX MEDLINE=91120847; PubMed=2126206; [NCBI, ExpASY, EBI, Israel, Japan]  
RA Dasgupta B.R., Dekleva M.L.;  
RT "Botulinum neurotoxin type A: sequence of amino acids at the  
RT N-terminus and around the nicking site.";  
RL Biochimie 72:661-664(1990).  
RN [9]  
RP SEQUENCE OF 448-464 AND 872-895.  
RX MEDLINE=89024662; PubMed=3178218; [NCBI, ExpASY, EBI, Israel, Japan]  
RA Sathymoorthy V., Dasgupta B.R., Foley J., Niece R.L.;  
RT "Botulinum neurotoxin type A: cleavage of the heavy chain into two  
RT halves and their partial sequences.";  
RL Arch. Biochem. Biophys. 266:142-151(1988).  
RN [10]  
RP SEQUENCE OF 448-482.  
RX MEDLINE=85285016; PubMed=3896784; [NCBI, ExpASY, EBI, Israel, Japan]  
RA Shone C.C., Hambleton P., Melling J.;  
RT "Inactivation of Clostridium botulinum type A neurotoxin by trypsin  
RT and purification of two tryptic fragments. Proteolytic action near  
RT the COOH-terminus of the heavy subunit destroys toxin-binding  
RT activity.";  
RL Eur. J. Biochem. 151:75-82(1985).  
RN [11]  
RP IDENTIFICATION OF SUBSTRATE.  
RX MEDLINE=94063091; PubMed=8243676; [NCBI, ExpASY, EBI, Israel, Japan]  
RA Schiavo G., Santtuci A., Dasgupta B.R., Mehta P.P., Jontes J.,  
RA Benfenati F., Wilson M.C., Montecucco C.;  
RT "Botulinum neurotoxins serotypes A and E cleave SNAP-25 at distinct  
RT COOH-terminal peptide bonds.";  
RL FEBS Lett. 335:99-103(1993).  
RN [12]  
RP IDENTIFICATION OF SUBSTRATE.  
RX MEDLINE=94124495; PubMed=8294407; [NCBI, ExpASY, EBI, Israel, Japan]  
RA Binz T., Blasi J., Yamasaki S., Baumeister A., Link E., Suedhof T.C.,  
RA Jahn R., Niemann H.;  
RT "Proteolysis of SNAP-25 by types E and A botulinum neurotoxins.";  
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RN [13]  
 RP MUTAGENESIS OF GLU-261; PHE-265 AND TYR-365.  
 RX MEDLINE=21556941; PubMed=11700044; [NCBI, ExpASY, EBI, Israel, Japan]  
 RA Rigoni M., Caccin P., Johnson E.A., Montecucco C., Rossetto O.;  
 RT "Site-directed mutagenesis identifies active-site residues of the  
 RT light chain of botulinum neurotoxin type a."  
 RL Biochem. Biophys. Res. Commun. 288:1231-1237(2001).

RN [14]  
 RP X-RAY CRYSTALLOGRAPHY (3.3 ANGSTROMS).  
 RX MEDLINE=98455071; PubMed=9783750; [NCBI, ExpASY, EBI, Israel, Japan]  
 RA Lacy D.B., Tepp W., Cohen A.C., Dasgupta B.R., Stevens R.C.;  
 RT "Crystal structure of botulinum neurotoxin type A and implications  
 RT for toxicity."  
 RL Nat. Struct. Biol. 5:898-902(1998).  
 CC -!- FUNCTION: Inhibits acetylcholine release. The botulinum toxin  
 CC binds with high affinity to peripheral neuronal presynaptic  
 CC membrane, is then internalized by receptor-mediated endocytosis.  
 CC The C-terminus of the heavy chain (H) is responsible for the  
 CC adherence of the toxin to the cell surface while the N-terminus  
 CC mediates transport of the light chain from the endocytic vesicle  
 CC to the cytosol. After translocation, the light chain (L)  
 CC hydrolyzes the 197-Gln-|-Arg-198 bond in SNAP-25, thereby blocking  
 CC neurotransmitter release. Inhibition of acetylcholine release  
 CC results in flaccid paralysis, with frequent heart or respiratory  
 CC failure.  
 CC -!- CATALYTIC ACTIVITY: Limited hydrolysis of proteins of the  
 CC neuroexocytosis apparatus, synaptobrevins, SNAP25 or syntaxin. No  
 CC detected action on small molecule substrates.  
 CC -!- SUBUNIT: Disulfide-linked heterodimer of a light chain (L) and a  
 CC heavy chain (H).  
 CC -!- SUBCELLULAR LOCATION: Secreted.  
 CC -!- PHARMACEUTICAL: Available under the name BOTOX (Allergan) for  
 CC the treatment of strabismus and blepharospasm associated with  
 CC dystonia and cervical dystonia. Also used for the treatment of  
 CC hemifacial spasm and a number of other neurological disorders  
 CC characterized by abnormal muscle contraction.  
 CC -!- MISCELLANEOUS: There are seven antigenically distinct forms of  
 CC botulinum neurotoxin: Types A, B, C1, D, E, F, and G.  
 CC -!- SIMILARITY: BELONGS TO PEPTIDASE FAMILY M27.  
 CC -!- DATABASE: NAME=BOTOX product information Web site;  
 CC WWW="<http://www.botox.com/index.jsp?hp&productinfo>".  
 CC -!- DATABASE: NAME=Protein Spotlight;  
 CC NOTE=Issue 19 of February 2002;  
 CC WWW="<http://www.expasy.org/spotlight/articles/sptlt019.html>".

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 CC -----

DR EMBL; X52066; CAA36289.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]  
 DR EMBL; M30196; AAA23262.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]  
 DR EMBL; X92973; CAA63551.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]  
 DR EMBL; D67030; BAA11051.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]  
 DR EMBL; M27892; AAA23269.1; -. [EMBL / GenBank / DDBJ] [CoDingSequence]  
 DR PIR; A35294; BTCLAB.  
 DR PIR; S09492; S09492.



DR PDB; 3BTA; 01-OCT-99. [ExpASY / RCSB]  
 DR MEROPS; M27.002; -.  
 DR InterPro; IPR000395; Bontoxilysin.  
 DR InterPro; IPR000130; Zn MTpeptdse.  
 DR InterPro; Graphical view of domain structure.  
 DR Pfam; PF01742; Peptidase M27; 1.  
 DR PRINTS; PR00760; BONTOXILYSIN.  
 DR ProDom; PD001963; Bontoxilysin; 1.  
 DR ProDom [Domain structure / List of seq. sharing at least 1 domain ]  
 DR PROSITE; PS00142; ZINC\_PROTEASE; 1.  
 DR BLOCKS; P10845.  
 DR ProtoNet; P10845.  
 DR ProtoMap; P10845.  
 DR PRESAGE; P10845.  
 DR DIP; P10845.  
 DR ModBase; P10845.  
 DR SWISS-2DPAGE; GET REGION ON 2D PAGE.  
 KW Neurotoxin; Transmembrane; Hydrolase; Metalloprotease; Zinc;  
 KW Pharmaceutical; 3D-structure.  
 FT INIT\_MET 0 0  
 FT CHAIN 1 447 BOTULINUM NEUROTOXIN A, LIGHT-CHAIN.  
 FT CHAIN 448 1295 BOTULINUM NEUROTOXIN A, HEAVY-CHAIN.  
 FT METAL 222 222 ZINC (CATALYTIC).  
 FT ACT\_SITE 223 223  
 FT METAL 226 226 ZINC (CATALYTIC).  
 FT METAL 261 261 ZINC (CATALYTIC).  
 FT DISULFID 429 453 INTERCHAIN.  
 FT DISULFID 1234 1279  
 FT TRANSMEM 626 646 POTENTIAL.  
 FT TRANSMEM 655 675 POTENTIAL.  
 FT VARIANT 26 26 V -> A.  
 FT MUTAGEN 261 261 E->A: DRASTIC DECREASE IN ENZYMATIC  
 FT ACTIVITY.  
 FT MUTAGEN 265 265 F->A: DECREASE IN ENZYMATIC ACTIVITY.  
 FT MUTAGEN 365 365 Y->A: DECREASE IN ENZYMATIC ACTIVITY.  
 FT CONFLICT 1 1 P -> Q (IN REF. 1).  
 FT CONFLICT 479 479 E -> P (IN REF. 9).  
 FT CONFLICT 875 875 T -> L (IN REF. 8).  
 FT CONFLICT 891 891 S -> K (IN REF. 8).  
 SQ SEQUENCE 1295 AA; 149322 MW; 858342F754862579 CRC64;  
 PFVFNKQFNKYK DPNVNGVDIAY IKIPNVGQMQ PVKAFKIHNK IWVIPERDTF TNPEEGDLNP  
 PPEAKQVPVS YYDSTYLSTD NEKDNYLKGK TKLFERIYST DLGRMLLTSI VRGIPFWGGS  
 TIDTELKVID TNCINVIQPD GSYRSEELNL VIIGPSADII QFECKSFGHE VLNLTRNGYG  
 STQYIRFSPD FTFGFEESE VDTNPLLGG KFDATDPAVTL AHELIHAGHR LYGIAINPNR  
 VFKVNTNAYY EMSGLEVSFE ELRTFGGHDA KFIDSLQENE FRLYYYNKKF DIASLTNLKAK  
 SIVGTTASLQ YMKNVFKEY LLSSETSGKF SVDKLFKFDK YKMLTEIYTE DNFVKKFKVL  
 NRKTYLNFDF AVFKINIVPK VNYTIYDGFN LRNTNLAAFN NGQNTTEINM NFTKLKNFTG  
 LFEFYKLLCV RGIITSKTKS LDKGYNKALN DLCKVNNWD LFFSPSEDNF TNDLNKGEEI  
 TSDTNIEAAE ENISLDLIQQ YYLTFNFDNE PENISIENLS SDIIGQLELM PNIERFPNGK  
 KYELDKYTMF HYLRAQEFH GKSRIALTNS VNEALLNPSR VYTFSSDYV KKVNKATEAA  
 MFLGWVEQLV YDFTDETSEV STTDKIADIT IIPYIGPAL NIGNMLYKDD FVGALIFSGA  
 VILLEFIPEI AIPVLGTFAL VSYIANKVLT VQTIDNALS RNEKWDEVYK YIVTNWLAKV  
 NTQIDLIRKK MKEALENQAE ATKAIINYQY NQYTEEEKNN INFNIDDLSS KLNESINKAM  
 ININKFLNQC SVSYLMNSMI PYGKVRLEDF DASLKDALLK YIYDNRGTI GQVDRLLKDKV  
 NNTLSTDIPF QLSKYVDNQR LLSTFTEYIK NIINTSILNL RYESNHLIDL SRYASKINIG  
 SKVNFDPIDK NQIQLFNLES SKIEVILKNA IVYNSMYENF STSFWIRIPK YFNSISLNNE  
 YTIINCMEEN SGWKVSLNYG EIIWTLQDTQ EIKQRVVFKY SQMINISDYI NRWIFVTITN  
 NRLNNSKIYI NGRLLIDQKPI SNLGNHASN NIMFKLDGCR DTHRYIWIY FNLFDKELNE  
 KEIKDLYDNQ SNSGILKDFW GDYLQYDKPY YMLNLYDPNK YVDVNNVGIR GMYLKGPRG  
 SVMTTNIYLN SSLYRGTKFI IKKYASGNKD NIVRNNDRVY INVVKVKEY RLATNASQAG

VEKILSALEI PDVGNLSQVV VMKSKNDQGI TNKCKMNLQD NNGNDIGFIG FHQFNNTAKL  
VASNWNRYQI ERSSRTLGCW WEFIPVDDGW GERPL

//

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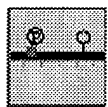
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[ScanProsite](#), [MotifScan](#)



Tools Sequence analysis tools: [ProtParam](#), [ProtScale](#),  
[Compute pI/Mw](#), [PeptideMass](#), [PeptideCutter](#),  
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